

*Sandals, William***ENTERED**#7
P

1600

RAW SEQUENCE LISTING

DATE: 04/04/2003

PATENT APPLICATION: US/10/054,435A

TIME: 11:20:49

Input Set : N:\Crf3\RULE60\10054435.raw.txt

Output Set: N:\CRF4\04042003\J054435A.raw

```

1 <110> APPLICANT: Bollag, Gideon
2      Crompton, Anne
3      North, Anne
4      Sharma, Sanju
5      Roscoe, William
6 <120> TITLE OF INVENTION: Methods and Compositions for Treating Abnormal Cell
7      Growth Related to Unwanted Guanine Nucleotide Exchange
8      Factor Activity
9 <130> FILE REFERENCE: 1028-US
10 <140> CURRENT APPLICATION NUMBER: US/10/054,435A
11 <141> CURRENT FILING DATE: 2002-01-18
12 <150> PRIOR APPLICATION NUMBER: US/09/079,812E
13 <151> PRIOR FILING DATE: 1998-05-15
14 <150> PRIOR APPLICATION NUMBER: 60/049,879
15 <151> PRIOR FILING DATE: 1997-06-17
16 <160> NUMBER OF SEQ ID NOS: 33
17 <170> SOFTWARE: PatentIn Ver. 2.0
19 <210> SEQ ID NO: 1
20 <211> LENGTH: 3171
21 <212> TYPE: DNA
22 <213> ORGANISM: Liver Rac GEF
23 <220> FEATURE:
24 <221> NAME/KEY: CDS
W--> 25 <222> LOCATION: Complement (76)..(2208)
26 <400> SEQUENCE: 1
27      tcactcaaac cagtgaagct tgggaaagtc attgacctcc agtcgttctg ctgagaaaca 60
28      tctggctcta ttcc atg gag acc agg gaa tct gaa gat ttg gaa aag acc 111
W--> 29      Met Glu Thr Arg Glu Ser Glu Asp Leu Glu Lys Thr
30      1              5              10
31      cgg agg aaa tca gca agt gat caa tgg aac act gat aat gaa cca gcc 159
32      Arg Arg Lys Ser Ala Ser Asp Gln Trp Asn Thr Asp Asn Glu Pro Ala
33      15              20              25
34      aag gtg aaa cct gag tta ctc cca gaa aaa gag gag act tct caa gct 207
35      Lys Val Lys Pro Glu Leu Leu Pro Glu Lys Glu Glu Thr Ser Gln Ala
36      30              35              40
37      gac cag gat atc caa gac aaa gag cct cat tgc cac atc cca att aag 255
38      Asp Gln Asp Ile Gln Asp Lys Glu Pro His Cys His Ile Pro Ile Lys
39      45              50              55              60
40      aga aat tcc atc ttc aat cgc tcc ata aga cgc aaa agc aaa gcc aag 303
41      Arg Asn Ser Ile Phe Asn Arg Ser Ile Arg Arg Lys Ser Lys Ala Lys
42      65              70              75
43      gcc aga gac aac ccc gaa cgg aac gcc agc tgc ctg gca gat tca cag 351
44      Ala Arg Asp Asn Pro Glu Arg Asn Ala Ser Cys Leu Ala Asp Ser Gln

```

RAW SEQUENCE LISTING

DATE: 04/04/2003

PATENT APPLICATION: US/10/054,435A

TIME: 11:20:49

Input Set : N:\Crif3\RULE60\10054435.raw.txt

Output Set: N:\CRF4\04042003\J054435A.raw

45		80		85		90		
46	gac aat gga	aaa tct gta aat	gag ccc ctg acc ttg aat atc ccc tgg	399				
47	Asp Asn Gly	Lys Ser Val Asn	Glu Pro Leu Thr Leu Asn Ile Pro Trp					
48		95	100	105				
49	agc aga atg	cct cct tgc aga aca gca atg cag aca gac cca gga gcc	447					
50	Ser Arg Met	Pro Pro Cys Arg	Thr Ala Met Gln Thr Asp Pro Gly Ala					
51		110	115	120				
52	cag gaa atg	agt gag tgc tcc tcc acc ccg gga aat ggg gcc acg ccc	495					
53	Gln Glu Met	Ser Glu Ser Ser Ser Thr Pro Gly Asn Gly Ala Thr Pro						
54		125	130	135				
55	gag gag tgg	ccg gcc ctg gcc gac agc ccc acc acg ctc acc gag gcc	543					
56	Glu Glu Trp	Pro Ala Leu Ala Asp Ser Pro Thr Thr Leu Thr Glu Ala						
57		145	150	155				
58	ctg cgg atg	atc cac ccc att ccc gcc gac tcc tgg aga aac ctc att	591					
59	Leu Arg Met	Ile His Pro Ile Pro Ala Asp Ser Trp Arg Asn Leu Ile						
60		160	165	170				
61	gaa caa ata	ggg ctc ctg tat cag gaa tac cga gat aaa tgc act ctc	639					
62	Glu Gln Ile	Gly Leu Leu Tyr Gln Glu Tyr Arg Asp Lys Ser Thr Leu						
63		175	180	185				
64	caa gaa atc	gaa acc agg agg caa cag gat gca gaa ata gaa gac aat	687					
65	Gln Glu Ile	Glu Thr Arg Arg Gln Gln Asp Ala Glu Ile Glu Asp Asn						
66		190	195	200				
67	acc aat ggg	tcc ccg gcc agt gag gac acc ccg gag gag gaa gaa gaa	735					
68	Thr Asn Gly	Ser Pro Ala Ser Glu Asp Thr Pro Glu Glu Glu Glu Glu						
69		205	210	215				
70	gag gag gag	gag gag ccg gcc agc cca cca gag agg aag act ctg	783					
71	Glu Glu Glu	Glu Glu Pro Ala Ser Pro Pro Glu Arg Lys Thr Leu						
72		225	230	235				
73	ccc cag atc	tgc ctg ctc agt aac ccc cac tca agg ttc aac ctc tgg	831					
74	Pro Gln Ile	Cys Leu Leu Ser Asn Pro His Ser Arg Phe Asn Leu Trp						
75		240	245	250				
76	cag gat ctt	ccc gag atc cgg agc agc ggg gtg ctt gag atc cta cag	879					
77	Gln Asp Leu	Pro Glu Ile Arg Ser Ser Gly Val Leu Glu Ile Leu Gln						
78		255	260	265				
79	cct gag gag	att aag ctg cag gag gcc atg ttc gag ctg gtc act tcc	927					
80	Pro Glu Glu	Ile Lys Leu Gln Glu Ala Met Phe Glu Leu Val Thr Ser						
81		270	275	280				
82	gag gcg tcc	tac tac aag agt ctg aac ctg ctc gtg tcc cac ttc atg	975					
83	Glu Ala Ser	Tyr Tyr Lys Ser Leu Asn Leu Leu Val Ser His Phe Met						
84		285	290	295				
85	gag aac gag	cgg ata agg aag atc ctg cac ccg tcc gag gcg cac atc	1023					
86	Glu Asn Glu	Arg Ile Arg Lys Ile Leu His Pro Ser Glu Ala His Ile						
87		305	310	315				
88	ctc ttc tcc	aac gtc ctg gac gtg ctg gct gtc agt gag cgg ttc ctc	1071					
89	Leu Phe Ser	Asn Val Leu Asp Val Leu Ala Val Ser Glu Arg Phe Leu						
90		320	325	330				
91	ctg gag ctg	gag cac cgg atg gag gag aac atc gtc atc tct gac gtg	1119					
92	Leu Glu Leu	Glu His Arg Met Glu Glu Asn Ile Val Ile Ser Asp Val						
93		335	340	345				

RAW SEQUENCE LISTING

DATE: 04/04/2003

PATENT APPLICATION: US/10/054,435A

TIME: 11:20:49

Input Set : N:\Crf3\RULE60\10054435.raw.txt

Output Set: N:\CRF4\04042003\J054435A.raw

94	tgt gac atc gtg tac cgt tat gcg gcc gac cac ttc tct gtc tac atc	1167
95	Cys Asp Ile Val Tyr Arg Tyr Ala Ala Asp His Phe Ser Val Tyr Ile	
96	350 355 360	
97	acc tac gtc agc aat cag acc tac cag gag cgg acc tat aag cag ctg	1215
98	Thr Tyr Val Ser Asn Gln Thr Tyr Gln Glu Arg Thr Tyr Lys Gln Leu	
99	365 370 375 380	
100	ctc cag gag aag gca gct ttc cgg gag ctg atc gcg cag cta gag ctc	1263
101	Leu Gln Glu Lys Ala Ala Phe Arg Glu Leu Ile Ala Gln Leu Glu Leu	
102	385 390 395	
103	gac ccc aag tgc agg ggg ctg ccc ttc tcc tcc ttc ctc atc ctg cct	1311
104	Asp Pro Lys Cys Arg Gly Leu Pro Phe Ser Ser Phe Leu Ile Leu Pro	
105	400 405 410	
106	ttc cag agg atc aca cgc ctc aag ctg ttg gtc cag aac atc ctg aag	1359
107	Phe Gln Arg Ile Thr Arg Leu Lys Leu Leu Val Gln Asn Ile Leu Lys	
108	415 420 425	
109	agg gta gaa gag agg tct gag cgg gag tgc act gct ttg gat gct cac	1407
110	Arg Val Glu Glu Arg Ser Glu Arg Glu Cys Thr Ala Leu Asp Ala His	
111	430 435 440	
112	aag gag ctg gaa atg gtg gtg aag gca tgc aac gag ggc gtc agg aaa	1455
113	Lys Glu Leu Glu Met Val Val Lys Ala Cys Asn Glu Gly Val Arg Lys	
114	445 450 455 460	
115	atg agc cgc acg gaa cag atg atc agc att cag aag aag atg gag ttc	1503
116	Met Ser Arg Thr Glu Gln Met Ile Ser Ile Gln Lys Lys Met Glu Phe	
117	465 470 475	
118	aag atc aag tgc gtg ccc atc atc tcc cac tcc cgc tgg ctg ctg aag	1551
119	Lys Ile Lys Ser Val Pro Ile Ile Ser His Ser Arg Trp Leu Leu Lys	
120	480 485 490	
121	cag ggt gag ctg cag cag atg tca ggc ccc aag acc tcc cgg acc ctg	1599
122	Gln Gly Glu Leu Gln Gln Met Ser Gly Pro Lys Thr Ser Arg Thr Leu	
123	495 500 505	
124	agg acc aag aag ctc ttc cac gaa att tac ctc ttc ctg ttc aac gac	1647
125	Arg Thr Lys Lys Leu Phe His Glu Ile Tyr Leu Phe Leu Phe Asn Asp	
126	510 515 520	
127	ctg ctg gtg atc tgc cgg cag att cca gga gac aag tac cag gta ttt	1695
128	Leu Leu Val Ile Cys Arg Gln Ile Pro Gly Asp Lys Tyr Gln Val Phe	
129	525 530 535 540	
130	gac tca gct ccg cgg gga ctg ctg cgt gtg gag gag ctg gag gac cag	1743
131	Asp Ser Ala Pro Arg Gly Leu Leu Arg Val Glu Glu Leu Glu Asp Gln	
132	545 550 555	
133	ggc cag acg ctg gcc aac gtg ttc atc ctg cgg ctg ctg gag aac gca	1791
134	Gly Gln Thr Leu Ala Asn Val Phe Ile Leu Arg Leu Leu Glu Asn Ala	
135	560 565 570	
136	gat gac cgg gag gcc acc tac atg cta aag gcg tcc tct cag agt gag	1839
137	Asp Asp Arg Glu Ala Thr Tyr Met Leu Lys Ala Ser Ser Gln Ser Glu	
138	575 580 585	
139	atg aag cgt tgg atg acc tca ctg gcc ccc aac agg agg acc aag ttt	1887
140	Met Lys Arg Trp Met Thr Ser Leu Ala Pro Asn Arg Arg Thr Lys Phe	
141	590 595 600	
142	gtt tgc ttc aca tcc cgg ctg ctg gac tgc ccc cag gtc cag tgc gtg	1935

RAW SEQUENCE LISTING

DATE: 04/04/2003

PATENT APPLICATION: US/10/054,435A

TIME: 11:20:49

Input Set : N:\Crif3\RULE60\10054435.raw.txt

Output Set: N:\CRF4\04042003\J054435A.raw

```

143      Val Ser Phe Thr Ser Arg Leu Leu Asp Cys Pro Gln Val Gln Cys Val
144      605                               610                               615                               620
145      cac cca tac gtg gct cag cag cca gac gag ctg acg ctg gag ctc gcc      1983
146      His Pro Tyr Val Ala Gln Gln Pro Asp Glu Leu Thr Leu Glu Leu Ala
147                               625                               630                               635
148      gac atc ctc aac atc ctg gac aag act gac gac ggg tgg atc ttt ggc      2031
149      Asp Ile Leu Asn Ile Leu Asp Lys Thr Asp Asp Gly Trp Ile Phe Gly
150                               640                               645                               650
151      gag cgt ctg cac gac cag gag aga ggc tgg ttc ccc agc tcc atg act      2079
152      Glu Arg Leu His Asp Gln Glu Arg Gly Trp Phe Pro Ser Ser Met Thr
153                               655                               660                               665
154      gag gag atc ttg aat ccc aag atc cgg tcc cag aac ctc aag gaa tgt      2127
155      Glu Glu Ile Leu Asn Pro Lys Ile Arg Ser Gln Asn Leu Lys Glu Cys
156      670                               675                               680
157      ttc cgt gtc cac aag atg gat gac cct cag cgc agc cag aac aag gac      2175
158      Phe Arg Val His Lys Met Asp Asp Pro Gln Arg Ser Gln Asn Lys Asp
159      685                               690                               695                               700
160      cgc agg aag ctg ggc agc cgg aat cgg caa tga cccccaccca gggggccagc      2228
161      Arg Arg Lys Leu Gly Ser Arg Asn Arg Gln
162                               705                               710
163      gggagcaggg cctgcatgag accccgacag aaggtggggg gggggggggg ggctctggga      2288
164      agcacaggcc agcacctccc caggtggcag gatctggctt ggggtgcccg gccctcatcc      2348
165      ctgcccacgc agtgagtgtc catgtgtctt ggccccttgc tcgcaaactg gataaagggg      2408
166      gcccaagcct ctctgatgac atttgtaaac aagaagggtt cagcagtatt acaccacctc      2468
167      cctcatgcct ccgagggggg ggaagggggg gggcacactc cagggccccc catgcccctg      2528
168      gccccaggg attggaagag gctcccaacc cagagtgtcc ctgtgggagg caggcagaag      2588
169      gtgacaattg acacgatttc ctgcacgcgt cttcttttac cttggaagca gttagaattt      2648
170      accaggcaca gatgaggccg cccttgccctg acggagcttg atgagcagcc cttggtctcc      2708
171      ggttcagga ctgagagccc agctgcctct gccaccctt cccagggcct ctgccagcct      2768
172      ctggctgcac ggtcaggccc tgcccctatg caggcctgcc agagcttggc tggggacccc      2828
173      tcccgcctct ggctccctga tgggctggat gtaacttggt tcttctagcc ccttaaggag      2888
174      cccaggtgtt ttaaggaatg aattggcacc tgcacttggt atcgattatg gttctgagaa      2948
175      aagcaaatat cggaattcct gcagcccggg aaatggggcc acgcccagg agtggccggc      3008
176      cctggccgac agccccacca cgctcaccga ggccctgcgg atgateccac ccattcccgc      3068
177      cgactcctgg agaaacctca ttgaacaaat agggctcctg tatcaggaat accgagataa      3128
178      atcgactctc caaaaaaaaaa aaaaaaaaaa gatctttaat taa      3171
180 <210> SEQ ID NO: 2
181 <211> LENGTH: 710
182 <212> TYPE: PRT
183 <213> ORGANISM: Liver Rac GEF
184 <400> SEQUENCE: 2
185      Met Glu Thr Arg Glu Ser Glu Asp Leu Glu Lys Thr Arg Arg Lys Ser
186      1                               5                               10                               15
187      Ala Ser Asp Gln Trp Asn Thr Asp Asn Glu Pro Ala Lys Val Lys Pro
188      20                               25                               30
189      Glu Leu Leu Pro Glu Lys Glu Glu Thr Ser Gln Ala Asp Gln Asp Ile
190      35                               40                               45
191      Gln Asp Lys Glu Pro His Cys His Ile Pro Ile Lys Arg Asn Ser Ile
192      50                               55                               60

```

RAW SEQUENCE LISTING

DATE: 04/04/2003

PATENT APPLICATION: US/10/054,435A

TIME: 11:20:49

Input Set : N:\Crf3\RULE60\10054435.raw.txt

Output Set: N:\CRF4\04042003\J054435A.raw

```

193 Phe Asn Arg Ser Ile Arg Arg Lys Ser Lys Ala Lys Ala Arg Asp Asn
194 65 70 75 80
195 Pro Glu Arg Asn Ala Ser Cys Leu Ala Asp Ser Gln Asp Asn Gly Lys
196 85 90 95
197 Ser Val Asn Glu Pro Leu Thr Leu Asn Ile Pro Trp Ser Arg Met Pro
198 100 105 110
199 Pro Cys Arg Thr Ala Met Gln Thr Asp Pro Gly Ala Gln Glu Met Ser
200 115 120 125
201 Glu Ser Ser Ser Thr Pro Gly Asn Gly Ala Thr Pro Glu Glu Trp Pro
202 130 135 140
203 Ala Leu Ala Asp Ser Pro Thr Thr Leu Thr Glu Ala Leu Arg Met Ile
204 145 150 155 160
205 His Pro Ile Pro Ala Asp Ser Trp Arg Asn Leu Ile Glu Gln Ile Gly
206 165 170 175
207 Leu Leu Tyr Gln Glu Tyr Arg Asp Lys Ser Thr Leu Gln Glu Ile Glu
208 180 185 190
209 Thr Arg Arg Gln Gln Asp Ala Glu Ile Glu Asp Asn Thr Asn Gly Ser
210 195 200 205
211 Pro Ala Ser Glu Asp Thr Pro Glu Glu Glu Glu Glu Glu Glu Glu
212 210 215 220
213 Glu Glu Pro Ala Ser Pro Pro Glu Arg Lys Thr Leu Pro Gln Ile Cys
214 225 230 235 240
215 Leu Leu Ser Asn Pro His Ser Arg Phe Asn Leu Trp Gln Asp Leu Pro
216 245 250 255
217 Glu Ile Arg Ser Ser Gly Val Leu Glu Ile Leu Gln Pro Glu Glu Ile
218 260 265 270
219 Lys Leu Gln Glu Ala Met Phe Glu Leu Val Thr Ser Glu Ala Ser Tyr
220 275 280 285
221 Tyr Lys Ser Leu Asn Leu Leu Val Ser His Phe Met Glu Asn Glu Arg
222 290 295 300
223 Ile Arg Lys Ile Leu His Pro Ser Glu Ala His Ile Leu Phe Ser Asn
224 305 310 315 320
225 Val Leu Asp Val Leu Ala Val Ser Glu Arg Phe Leu Leu Glu Leu Glu
226 325 330 335
227 His Arg Met Glu Glu Asn Ile Val Ile Ser Asp Val Cys Asp Ile Val
228 340 345 350
229 Tyr Arg Tyr Ala Ala Asp His Phe Ser Val Tyr Ile Thr Tyr Val Ser
230 355 360 365
231 Asn Gln Thr Tyr Gln Glu Arg Thr Tyr Lys Gln Leu Leu Gln Glu Lys
232 370 375 380
233 Ala Ala Phe Arg Glu Leu Ile Ala Gln Leu Glu Leu Asp Pro Lys Cys
234 385 390 395 400
235 Arg Gly Leu Pro Phe Ser Ser Phe Leu Ile Leu Pro Phe Gln Arg Ile
236 405 410 415
237 Thr Arg Leu Lys Leu Leu Val Gln Asn Ile Leu Lys Arg Val Glu Glu
238 420 425 430
239 Arg Ser Glu Arg Glu Cys Thr Ala Leu Asp Ala His Lys Glu Leu Glu
240 435 440 445
241 Met Val Val Lys Ala Cys Asn Glu Gly Val Arg Lys Met Ser Arg Thr

```

VERIFICATION SUMMARY

PATENT APPLICATION: US/10/054,435A

DATE: 04/04/2003

TIME: 11:20:50

Input Set : N:\Crf3\RULE60\10054435.raw.txt

Output Set: N:\CRF4\04042003\J054435A.raw

L:25 M:351 W: Sequence data Name/Key Feature Out-of-Range, SEQ ID#:1, CDS LOCATION: Complement (76)..(2208)

L:29 M:351 W: Sequence data Name/Key Feature Out-of-Range, SEQ ID#: 1, CDS LOCATION:0..76

L:472 M:351 W: Sequence data Name/Key Feature Out-of-Range, SEQ ID#:30, CDS LOCATION: Complement (1)..(198)